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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,497	03/16/2004	Matthew During	102182-0036	3969

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EXAMINER	
FALK, ANNE MARIE	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
04/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/802,497	DURING ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *1-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed January 7, 2008 (hereinafter referred to as "the response") has been entered. No claims were amended.

Accordingly, Claims 1-48 remain pending in the instant application.

In the response filed December 13, 2006 Applicants elected Group II, Claims 43-48. Because applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The elected invention is drawn to a vector comprising a nucleotide sequence encoding GAD. In the response filed March 23, 2007 Applicants confirmed their election.

Applicants further elected with traverse the species adeno-associated viral vector for prosecution on the merits. The traversal is on the grounds that the generic claims are patentable. This is not found persuasive because, contrary to Applicants' assertion, the rejections set forth below demonstrate that the generic claims are not allowable. When no generic claim is finally held to be allowable, the claims are restricted to the elected species. In the response filed March 23, 2007 Applicants confirmed their election.

Claims 1-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 13, 2006.

Accordingly, Claims 43-48 are examined herein.

The rejection of Claims 43-48 under 35 U.S.C. 103(a), as being unpatentable over U.S. 2004/0101514 A1 (Liu et al., priority to March 14, 2000), is withdrawn in view of the arguments set forth at pages 8-10 of the response, which demonstrate that the effective filing date of Liu et al. is May 1, 2003.

Claim Objections

Claims 43-48 remain objected to for encompassing non-elected subject matter. In view of the rejections of the generic claims, non-elected species should be deleted from the claims. Following an election of species requirement, when no generic claim is finally held to be allowable, the claims are restricted to the elected species. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-46 and 48 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of 'written description' inquiry, whatever is claimed" (see page 1117). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

The claims recite "a post-transcriptional regulatory element" but the specification only describes the woodchuck hepadnavirus postregulatory element (page 35, lines 4-8). The specification does not describe any other post-transcriptional regulatory element suitable for use in the claimed vector.

The Guidelines for Written Description specifically state that "[t]he claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art" (Federal Register, Vol. 66, No. 4, page 1105, column 1 and MPEP 2163(I)(A)). The post-transcriptional regulatory element recited in the claims is an essential element of the claimed invention.

Where the claims recite "a post-transcriptional regulatory element" the claims encompass a genus of genetic elements that are not described. Thus, the claims cover the use of a genus of genetic elements, while providing a description of only a single post-transcriptional regulatory element. Therefore, the specification fails to describe the entire genus of elements, as recited in the claims.

In evaluating whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only a single species is described. This clearly would not be considered a representative number of species. Next then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In the instant case, the requisite genetic element has not been described by relevant identifying characteristics. This limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of the entire genus of "post-transcriptional regulatory elements" covered by the claims, at the time the application was filed. Thus, it is concluded that the written description requirement is not satisfied for the claimed vector comprising any "post-transcriptional regulatory element."

Applicants are reminded that the written description requirement is severable from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), *cert.* denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991) (While acknowledging that some of its cases concerning the written description requirement and

the enablement requirement are confusing, the Federal Circuit reaffirmed that under 35 U.S.C. 112, first paragraph, the written description requirement is separate and distinct from the enablement requirement and gave an example thereof). An invention may be described without the disclosure being enabling (e.g., a chemical compound for which there is no disclosed or apparent method of making), and a disclosure could be enabling without describing the invention (e.g., a specification describing a method of making and using a paint composition made of functionally defined ingredients within broad ranges would be enabling for formulations falling within the description but would not describe any specific formulation). See *In re Armbruster*, 512 F.2d 676, 677, 185 USPQ 152, 153 (CCPA 1975).

At page 8 of the response, Applicants assert that Schambach et al. (November 2000) provides evidence that one of ordinary skill in the art would know how to use appropriate posttranscriptional regulatory elements in the construction of the vector of the invention. However, while the cited reference describes two additional posttranscriptional regulatory elements that enhance gene expression, the cited reference is a post-filing reference and therefore does not demonstrate what was conventional in the art at the time of filing. Accordingly, one of ordinary skill in the art would not have had the benefit of the teachings of the cited reference at the time of filing. The effective filing date of the instant application is May 23, 2000.

To the extent that the claimed compositions are not described in the instant disclosure, Claims 43-46 and 48 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Thus, the specification only provides an enabling disclosure for vectors comprising the woodchuck hepadnavirus post-transcriptional regulatory element.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 43-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. 2002/0028212 A1 (Geoffroy et al., filed March 21, 1995) in view of Loeb et al. (1999, Human Gene Therapy 10: 2295-2305).

Claims 43-48 are directed to a vector for expression of GAD in cells of the central nervous system comprising: a tissue specific promoter operably linked to a nucleotide sequence encoding GAD and a post-transcriptional regulatory element.

Geoffroy et al. disclose the construction of an adenovirus vector comprising a gene encoding GAD67 under the control of RSV-LTR (see Example 1). The reference further discloses that the RSV-LTR promoter is advantageous for the expression of GAD in nerve cells and that the neuron-specific enolase promoter is particularly advantageous for expression in nerve cells (paragraph 0028). The reference further discloses that AAV vectors are particularly useful because they integrate into the genome of cells, are not involved in pathologies in man, and infect a broad spectrum of cells (paragraphs 0023-0024 Geoffroy et al. further disclose that recombinant vectors encoding GAD are useful for treating and preventing degenerative neurological diseases (abstract and throughout specification).

Loeb et al. (1999) disclose enhanced expression of transgenes from adeno-associated virus vectors with the woodchuck hepatitis virus post-transcriptional regulatory element (WPRE). The reference further disclosed that the WPRE evolved to stimulate the expression of intronless viral messages. The authors recognized that this ability to enhance expression could be useful in nonviral and

heterologous viral gene delivery systems if it retained its function in these heterologous contexts. Accordingly, the authors analyzed the ability of WPRE to elevate the expression of a cDNA encoding the green fluorescent protein (GFP) in these contexts. They found that the WPRE can stimulate the expression of GFP when the gene is delivered by transfection or transduction with recombinant AAV. The authors note that their results demonstrate that the WPRE will be an effective tool for increasing the long-term expression of transgenes in gene therapy.

In view of the teachings of Geoffroy et al. to develop vectors, including AAV vectors, encoding GAD for treatment of degenerative neurological diseases, and further in view of the fact that the reference explicitly discloses that AAV vectors are particularly advantageous and that the neuron specific enolase (NSE) promoter is particularly advantageous for driving expression in nerve cells, one of skill in the art would have been motivated to follow the guidance in the reference to produce an AAV vector comprising an NSE promoter driving expression of a GAD coding sequence. The skilled artisan would have further been motivated to use the WPRE to further enhance expression of a GAD cDNA transgene, in view of the teachings of Loeb et al. One of skill in the art would have anticipated a reasonable expectation of success in producing the vectors because only standard molecular biology techniques are required to combine the various elements known in the prior art to produce the vector.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

No claims are allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk, Ph.D. whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632